

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Phillips AN, Cambiano V, Miners A, et al. Effectiveness and cost-effectiveness of potential responses to future high levels of transmitted HIV drug resistance in antiretroviral drug-naïve populations beginning treatment: modelling study and economic analysis. *Lancet HIV* 2014; published online Oct 14. [http://dx.doi.org/10.1016/S2352-3018\(14\)70021-9](http://dx.doi.org/10.1016/S2352-3018(14)70021-9).

Appendix

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1. Description of methods

HIV Synthesis Transmission Model

The HIV Synthesis transmission model is an individual-based stochastic model of heterosexual transmission, progression and treatment of HIV infection within a southern African context (1-3). Full updated model details are in the supplementary material for ref 3, but a brief description follows. All variables are updated in 3 month periods in the model, which includes an age- and gender- structure. Sexual risk behaviour is modelled as the number of condomless-sex short term partners and presence of a condomless-sex long-term partner in each period. In any given period, the probability of an uninfected person having a condomless-sex partner who is infected with HIV depends on their number of partners and on the prevalence of HIV amongst partnerships formed by those of the opposite gender, accounting for patterns of age mixing. Given exposure to an infected partner, the probability of transmission depends on the viral load level of the partner (obtained by sampling from the distribution of viral load levels in partnerships formed by HIV infected people, accounting for gender and age), on the estimated risk of transmission at that viral load, presence of a concurrent sexually transmitted infection and on gender. Emergence of resistance on ART is dependent on adherence and the current number of active drugs. Adherence is assumed to have several components, with a distribution across individuals of a life long tendency, and also in the extent of period to period variation. In addition, various factors can influence adherence, including the initial measurement of viral load > 1000 copies/mL which is assumed to lead to an increase in adherence (with new adherence level sampled from a Normal distribution with mean 90% and standard deviation 5%, and a 10 fold increase in the rate of restarting ART in those who have interrupted) in 70% of people as a result of targeted adherence intervention; this is consistent with data showing that a high proportion of people with measured viral load > 1000 copies/mL subsequently achieve viral suppression without a change in ART (4-6). The appropriate duration to assume for this effect is uncertain and the impact of adherence interventions has often been shown to diminish with time (7). We assume that the adherence intervention is potentially effective only the first time it is performed and that for 40% the effect is permanent (28% of those with a viral load >1000 copies/mL), but that in the remaining 60% (42% of those with viral load >1000 copies/mL) it lasts only 6 months (except we assume the effect on restarting ART is permanent). We also model the possibility that in some individuals at certain times the adherence is so low that the individual has in fact interrupted ART, although this is undeclared to the clinic so the person is still considered by the clinic in any records kept as being on ART. Such a lack of adherence is thought to explain why some people have no resistance mutations present at virologic failure (8-10), and we mimic this in our model. Regarding resistance and transmission, the presence or not of resistance mutations does not influence the risk of transmission (i.e. virus with resistance mutations present is assumed equally transmissible as virus without such mutations, for a given viral load). For people who have become infected with HIV the variables modelled include viral load, CD4 cell count, presence of resistance mutations, risk of AIDS and death. Resistance is modelled in terms of the presence or not of specific mutations (e.g. number of thymidine analogue mutations (TAMS); presence of M184V (yes or no; y/n), K65R (y/n); L74V (y/n); Q151M (y/n), presence of a key NNRTI mutation (y/n); major PI mutations (y/n). Distinction is made for each mutation as to whether it is only present in minority virus

(if the patient has a mutation present but has stopped drugs that select for that mutation), so assumed not transmissible, or if it is present in majority virus, and hence assumed transmissible. For a newly infected person, the probability of being infected by a person with resistant virus as their majority virus population is determined by the probability, for the given viral load level of the person from whom the virus has been acquired, that drug resistance mutations are present in the concurrent infected population, again taking into account gender, age and number of partnerships formed. It is not assumed that all resistance mutations present in majority virus of the source partner are established as a mutation in virus in the newly infected person. This is dependent on the specific mutation. If a mutation is transmitted and established in the new host it is assumed to persist in majority virus but with a certain probability of loss of persistence in majority over time (11), but thereafter it remains in minority virus and is selected back as majority virus if relevant ART is initiated. We also consider the possibility of a person who is already infected become super-infected, including with drug resistant HIV (12). NNRTI-resistance acquired through use of nevirapine as PMTCT is assumed to eventually disappear even from minority virus.

The model structure used aims to capture the essence of the underlying biological mechanisms by which resistance and virologic failure arise, and is the result of careful consideration in discussion with virologists, clinicians and other modellers. The use of this structure means that few of the parameter values come directly from specific published values as estimates of the parameters relevant to our model structure are mostly not available. We have generated in the supplementary material to ref 3 a range of model outputs for comparison with published estimates to assess model calibration.

Programmatic scenarios modelled

In order to generate programmatic scenario scenarios with various levels of on-going TDR at t_0 – the time point at which the policy decision is being made (which was arbitrarily chosen as the year 2017) we varied many of the parameters that most strongly determine the level of TDR present in a population in 5000 model runs. These were: the adherence profile, the extent to which resistance mutations are transmitted (`res_trans_factor`; see model details), the rate with which transmitted mutations disappear from majority virus and become present only in minority virus (`rate_loss_persistence`), the underlying rate of interruption of ART (the actual rate at any point depends also on the average adherence (`adhav`) and presence of toxicity as well as this underlying rate; see model details), the probability of the drug supply being interrupted, and the rate of generation of new NNRTI drug resistance mutations as a result of interruption (due to the long tail in drug level). Distributions assumed for these are shown below under Parameters and Distributions. In order to generate programmatic scenarios with a high level of TDR we used a distribution of adherence patterns which includes a relatively high number of programmatic scenarios for which a high proportion of people have poor adherence. In such programmatic scenarios the proportion of people on ART with VL suppressed is low and the death rate of those on ART high. Although there are relatively few data, the proportion of programmatic scenarios in sub Saharan Africa with these characteristics is probably lower than it is in our programmatic scenarios, but we wished to include a high proportion of programmatic scenarios in which levels of NNRTI TDR are high in order to study the effects of

potential new policies in this context. For all programmatic scenarios, we assume that ART (first line regimen consisting of stavudine, 3TC and nevirapine before mid-2010 and tenofovir, 3TC and nevirapine after mid-2010) is provided with use of CD4 cell count monitoring to decide on when to start ART (CD4 cell count 200 /mm³ from 2003; CD4 cell count 350 /mm³ from 2010, 500 cells /mm³ from 2017). We assume that up to t0 the CD4 cell count is used to monitor people on first line to determine eligibility for switch to second line (CD4 cell count < 100 cells/mm³, as in the DART trial (13)). In both cases we assume only a 3% chance of switch in each 3 month period after the criteria is fulfilled, to reflect the very low rates of switching seen in practice. Then at t0 for each of these programmatic scenarios we considered what would be the predicted outcomes over the following 15 years (i.e. to 2032) of potential policy options, according to the current level of NNRTI-resistance in people about to start ART, excluding women with previous antiretroviral therapy for PMTCT. The potential policies are as follows (i) current policy, (ii) change of the standard NNRTI-based regimen to a bPI-based first line regimen (with a second line involving continued use of a bPI (bPI) and replacement of the tenofovir with zidovudine), (iii) individual-level resistance testing prior to ART initiation to detect key NNRTI mutations to inform whether to use an NNRTI-based or PI-based regimen as first line, (iv) introduction of routine (6m, 12m and then annual) viral load monitoring, replacing CD4 cell count monitoring (so unlike in the first three policies, in which the above-described CD4 count monitoring is assumed to continue, the first failure criteria is two consecutive viral load values > 1000 copies/mL), or (v) measurement of viral load at 6 months after start of ART, with a repeat test at 1 year if the value is > 1000 copies/mL, and with first line failure being called if the level at one year is above 1000 cps/mL, but otherwise not replacing CD4 cell count monitoring. We assume that the rate of switching after failure criteria have been fulfilled is increased to 0.2 per 3 months after t0. These potential policies were formulated at a WHO working group meeting in 2012. We undertook 5000 model runs as a balance between having sufficient stability of estimates and feasibility of running very large numbers of simulations. In order to most clearly understand their impact we assume that policies are fully implemented immediately. The model was programmed in SAS 9.3.

Economic Analysis

All of the evaluated alternatives have different cost implications and the ability of health care systems to fund interventions differs widely. The health benefits associated with the alternative policies were estimated on the basis on quality adjusted life years (QALYs) lived. Costs were estimated based upon resource use in the delivery of the policies (e.g. number of viral load tests provided, first line drug regimen used) and associated unit costs (see below). The time horizon for the analyses is 2017-32, and both costs and health benefits are discounted to present value using a 3.5% per annum discount rate.

The expected costs and health outcomes (QALYs) associated with each of the policy alternatives can be compared to inform which is likely to represent best value from available resources. The results are presented in the form of a ranking of the net monetary benefit across all policy options. The net monetary benefit (NMB) is expressed as the QALYs associated with a policy, multiplied by a cost-effectiveness-threshold, less the costs of that policy. The cost-effectiveness-threshold represents the opportunity costs of resources required to fund the intervention, in terms of the health gains those

resources could generate if used for alternative purposes (14). Based on current evidence, the policy that generates the highest NMB should be adopted and can be expected to maximize health gains in the population (15,16). We provide results for a range of cost-effectiveness-thresholds. For the more poorly resourced health systems in sub Saharan a value of \$500 or even lower is probably realistic given that many interventions offering health gains at this amount or less remain unfunded.

We assume the objective is to maximize health. Policies are made subject to uncertainty and on the basis of best current evidence. In reality, policy-makers may have the option to undertake more research to guide policy (for instance to better understand the effectiveness of the interventions, or to obtain better estimates of TDR in the population). Furthermore, we assume that there are no costs incurred with the change in strategy beyond those included as depreciation costs in the unit cost estimates. If there are other irrecoverable costs to adopting new policies we assume that the interventions will be used for their full effective lifetimes. This could be important because the introduction of laboratory-based viral load monitoring and resistance testing, in particular, would require significant capital investment that may not be necessary if point of care alternatives become available in the near future.

We performed sensitivity analyses in which we changed the cost of viral load from the \$45 in the base scenario to \$15, in which we also changed the cost of resistance testing from \$250 to \$100 and in which we reduced the cost of the bPI by 50%. Also we considered a smaller effect of viral load measurement on adherence.

2. Supplementary tables and figures

Supplementary Table 1: Difference in discounted costs and QALYs over 15 years compared with no change in policy according to t0 level of NNRTI-resistance in ART initiators and new policy option. Mean over 5000 programmatic scenarios.

Level of NNRTI resistance at start of ART at t0	New policy option starting from t0			
	bPI first line regimen ⁺	Pre-ART resistance testing ⁺⁺	Viral load monitoring ⁺⁺⁺	Viral load test at 6 months after ART initiation ⁺⁺⁺⁺
Difference in discounted cost in 2013 \$ (over 15 years; mean over programmatic scenarios) compared with current policy				
Difference in discounted QALYs (mean over programmatic scenarios) compared with current policy				
< 5%	2,456,000 491	826,000 233	1,086,000 327	187,000 128
5%-10%	2,576,000 729	977,000 331	1,161,000 454	224,000 175
10%-15%	2,534,000 1171	1,137,000 490	1,192,000 740	306,000 366
15%-20%	2,443,000 1752	1,280,000 728	1,221,000 1174	441,000 674
20%-25%	2,521,000 2192	1,458,000 861	1,297,000 1505	555,000 867
25%-	2,691,000 2505	1,626,000 1070	1,390,000 1746	596,000 893

NNRTI = non-nucleoside reverse transcriptase; bPI = boosted protease inhibitor

+ change of the standard NNRTI-based regimen to a bPI-based first-line regimen

++ individual-level resistance testing prior to ART initiation to detect key NNRTI mutations to inform whether use of an NNRTI-based or bPI-based regimen is optimal as first-line treatment,

+++ introduction of routine (6m, 12m and then annual) viral load monitoring, replacing 6 monthly CD4 cell count monitoring

++++ a single routine measurement of viral load at 6 months after start of ART, with routine CD4 cell count monitoring. In this last scenario, if the viral load is > 1000 copies/mL, it is repeated 6 months later and if above 1000 copies/mL, a switch to second-line is effected.

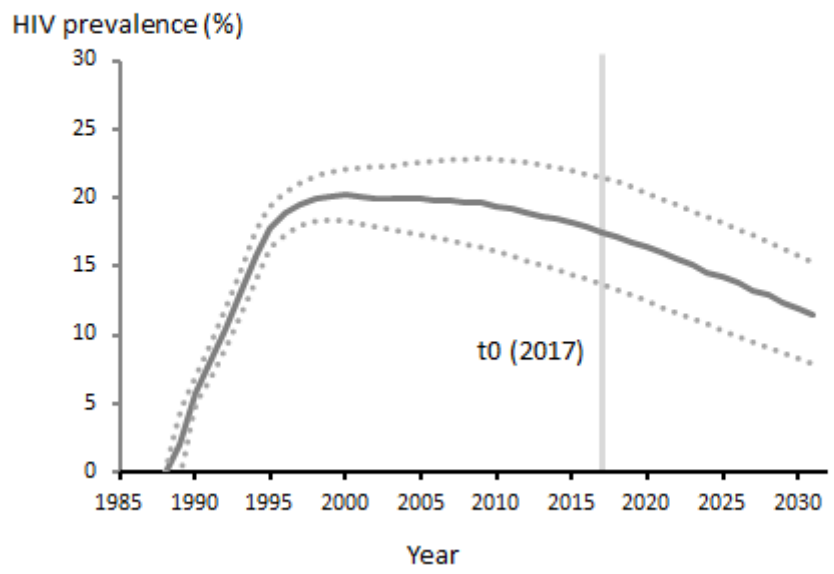
It should be noted that these are mean across all programmatic scenarios in each stratum of t0 level of NNRTI resistance at start of ART. Calculation of the net monetary benefit based on these means is a different approach to that used in Figure 2 of the main manuscript, where the policy with the highest net monetary benefit was calculated for each programmatic scenario and then the one that was most frequently the highest was declared to be the most cost-effective.

Supplementary Table 2: Median (90% range) % with adherence > 80% according to level of NNRTI-resistance at start of ART in 2017 (t0).

Level of NNRTI-resistance at start of ART in 2017

<5%	5%-	10%-	15%-	20%-	25%-
87% (78%-91%)	84% (72% - 90%)	77% (55% - 86%)	60% (42% - 81%)	54% (39% - 67%)	54% (38% - 65%)

Supplementary Figure 1. Median (90% range) prevalence over all 5000 programmatic scenarios, considering no change in policy after t0 (2017).



3. Parameter values and distributions

Details of variables are explained in Model details in Supplement to Ref 3.

Sexual behaviour

Sexual behaviour model structure: base structure ($rbm=4$)

Change in propensity to have a long term condomless sex partner after HIV diagnosis (ch_risk_diag): 9/13

Change in propensity to have short term (“new”) condomless sex partners after HIV diagnosis ($ch_risk_diag_newp$): 5/6

Date at which population level change in condomless sex behaviour occurs ($date_ch_risk_beh$): 1995

Change in propensity to have condomless sex (“risk behaviour”) with short term partners after threshold for population level change in condomless sex behaviour reached ($ch_risk_beh_newp$): Beta(50,70)

Change in propensity to have a long term condomless sex (“risk behaviour”) with short term partners after threshold for population level change in condomless sex behaviour reached ($ch_risk_beh_ep$): Beta(60,60)

Rate of starting new long term condomless sex partnership in 15-25 year age group ($eprate$): 0.1

Poisson mean for moderately high short term partner group (see model details) ($highsa$): 4.5

Poisson mean for highest short term partner group (see model details) (swn): 7

Factor to change overall average level of condomless sex with short term partners ($newp_factor$): 5.5

Proportion of the population who have a lifetime reduced number of condomless sex partners (see model details) (p_rred_p): 0.20

Probability per 3 months of pregnancy at age 35-45 ($prob_pregnancy_base$): 0.037

Fold difference in pregnancy rate at age: 15-25: 1.04; 25-35: 1.03; 45-55: 0.975

Transmission

Fold difference in transmission rate for a given viral load (see Model details for base assumption on transmission rate by viral load²): 1.0

Rate of transmission in primary HIV infection (lasting 3 months) ($tr_rate_primary$): 0.25

Transmission rate when plasma viral load is < 500 cps/mL ($tr_rate_undetec_vl$): 0.001

Fold higher rate of transmission from women to men, compared with men to women ($fold_change_w$): 1.5

Fold higher rate of transmission in young women compared with older women ($fold_change_yw$): 2.0

Fold higher rate of transmission if current STI present ($fold_change_sti$): 3.0

Fold lower transmission rate for short term partners compared with long term (reflecting average lower number of sex acts) ($fold_tr_newp$): 5/14

Super-infection: for people with HIV super-infected with a resistant virus, we assume a low (20%) probability that these mutations are established as resistance mutations.

Adjustment to factor determining extent to which some transmitted resistance is effectively immediately lost (even from minority virus) (res_trans_factor): lognormal(ln 0.8 ,0.20)

Probability per 3 months of loss of persistence of transmitted mutations from majority virus to minority virus (same for each mutation) (rate_loss_persistence): lognormal(ln 0.02,0.30)

Probability per 3 months of loss of NNRTI mutations, acquired due to PMTCT, from majority virus to become only in minority virus (rate_loss_nnres_pmtct_maj): 0.25

Probability per 3 months of loss of virus with NNRTI mutations acquired due to PMTCT, from minority virus to effectively be extinct altogether (rate_loss_nnres_pmtct_min): 0.25

Prevalence of male circumcision: 0.1

Date of introduction of VMMC: 2008

Rate of increase in probability of VM male circumcision per 3 months: (circ_inc_rate): lognormal(ln 0.003, 0.5)

HIV testing

Date start of testing (date_start_testing): 1996

Initial test probability for those with WHO condition (this increases by 0.008 per 3 mths after testing is introduced, up to 2015) (test_rate_who4): 0.2

Initial test probability for those with TB (this increases by 0.005 per 3 mths after testing is introduced, up to 2015) (test_rate_tb): 0.1

Initial test probability for those with current WHO 3 condition (this increases by 0.0012 per 3 mths after testing is introduced, up to 2015) (test_rate_who3): 0.03

Reduction in rate of testing if never had condomless sex (red_test_neversex): 0.33

Annual linear increase in testing (an_lin_incr_test): 0.000625 x 0.0025

Date start testing ANC (date_start_testanc): 1994

Rate test ANC (rate_testanc_inc): =0.0025

Fold difference in ANC testing rate by age:

fold_probanc_1519=0.73, fold_probanc_2024=1x1.36, fold_probanc_2529=0.9x1.14, fold_probanc_3039=0.8x1.00, fold_probanc_4049=0.70, fold_probanc_ov50=0.56

Natural progression

Probability of being lost (unlinked to care) at diagnosis (prob_loss_at_diag): 0.6

Initial CD4 count at infection (square root scale) (mean_sqrtcd4_inf): 27.5

Factor adjusting basic rate of natural cd4 decline (see model details) (fx): 1.0

Factor adjusting basic rate of natural viral load change (see model details) (gx): 1.0

Fold increase in risk of WHO 3 condition, compared with risk of WHO 4 condition, for given level of CD4 count, viral load and age (fold_incr_who3): 5

Fold decrease in risk of HIV-related death, compared with risk of WHO 4 condition, for given level of CD4 count, viral load and age (fold_decr_hivdeath): 0.25

Fold difference in risk of WHO 4 condition, for given level of CD4 count, viral load and age, compared with base assumption (see model details) (fold_change_in_risk_base_rate): 1.0

Increase in death rate in 3 months period in which a WHO 4 condition is present (incr_death_rate_adc): 5

Increase in death rate in 3 months period in which TB is present (incr_death_rate_tb): 2

Fold difference in non HIV related mortality, compared with base assumption (fold_change_ac_death_rate): 1

HIV monitoring, loss, return, interruption of art and restarting

Risk of loss to follow-up per 3 mths among those not on ART (rate_lost): 0.05

Probability of simultaneously being lost to follow-up amongst those stopping ART (prob_lost_art): 3/11

Probability (per 3 mths) of return to care for person lost (if no WHO 4 condition present – value is 1 if present) (rate_return): 0.05

Basic probability of restart of ART in those remaining under care who have stopped/interrupted ART (this is also influenced by presence of WHO 3 or 4 conditions) (rate_restart): 0.2

Probability of ART initiation per 3 months after eligibility fulfilled, if visting clinic: 0.5

ART

ART introduction date: 2003

Probability of switching to second line treatment, given first line failure (by whatever definition is being used) (pr_switch_line): 0.03 (changes to 0.2 after t0, 2017)

Pattern of adherence*: 1 20%, 2 20%, 3 20%, 4 20%, 5 20%.

Reduction in adherence resulting from presence of TB or a WHO 4 condition (red_adh_tb_adc): 0.1

Average reduction in adherence resuting from current toxicity (the actual reduction varies by individual person) (red_adh_tox_pop): 0.05

Additional "effective" adherence for people on NNRTI regimens due to longer half life (add_eff_adh_nnrti): 0.1

Average change in adherence on second line (degree of change varies by individual – note this can be a positive or negative change) (altered_adh_sec_line_pop) = 0.05

Proportion of people for whom a measured viral load > 1000 leads to an improvement in adherence (for the first time such a measurement is made only) (adh_effect_of_meas_alert): 0.7

Extent to which the CD4 change is more favourable on a virologically failing BPI-regimen compared with an NNRTI-regimen (poorer_cd4_rise_on_failing_nnrti): -6

Standard deviation for intra-subject variation in CD4 count (sd_cd4): 1.2

Standard deviation for the measurement error in CD4 count (sd_measured_cd4): 1.7

Base probability of interrupting ART per 3 mths (actual probability also depends on time on continuous ART, presence of current toxicity and average adherence – see model details) (rate_int_choice): lognormal(ln0.03, 0.30)

Probability of drug stock out, and hence ART interrupted (prob_supply_interrupted): lognormal(ln0.02, 0.30)

Probability that drug supply resumed during stock-out (prob_supply_resumed): 0.8

Probability of NNRTI-resistance emerging in women taking SD nevirapine for PMTCT: 0.35

Probability of NNRTI-resistance emerging in women taking nevirapine plus at least one other antiretroviral for PMTCT: 0.045

Fold difference in risk of mutations arising, for given number of active drugs, viral load and current adherence level, compared with base risk (see model details) (fold_change_mut_risk): 1

Similarly, specifically for thymidine analogue mutations: (fold_change_tams_risk): 1

Similarly, specifically for Q151M cross nucleoside resistance mutation: (fold_change_151_risk): 1

Standard deviation representing inter-patient variation in rate of CD4 rise - when CD4 is rising (sd_patient_cd4_rise_art): 0.2

Risk of NNRTI-resistance emergence due to stopping an NNRTI regimen (due to the tail in presence of drug meaning effective monotherapy): 0.03

Fraction of people who stop ART (and are still visiting the clinic) for whom the clinic is not aware of the interruption and is hence treating the patient as if they were on ART (and hence may switch to the next line having wrongly classified them as virologically failing): (clinic_not_aw_int_frac): 0.6

* There are various adherence pattern distributions (numbered 1-5) considered. *adhav* is an individual's average level of adherence and *adhvar* describes their period to period variability

Adherence pattern 1 (3% probability *adhav* = 0.50 *adhvar* = 0.2, 3% probability *adhav* = 0.80 *adhvar* = 0.2, 14% probability *adhav* = 0.90 *adhvar* = 0.06, 80% probability *adhav* = 0.95 *adhvar* = 0.05).

Adherence pattern 2 (5% probability *adhav* = 0.50 *adhvar* = 0.2, 10% probability *adhav* = 0.80 *adhvar* = 0.2, 27% probability *adhav* = 0.90 *adhvar* = 0.06, 38% probability *adhav* = 0.90 *adhvar* = 0.05, 20% probability *adhav* = 0.95 *adhvar* = 0.05)

Adherence pattern 3 (15% probability *adhav* = 0.50 *adhvar* = 0.2, 15% probability *adhav* = 0.70 *adhvar* = 0.2, 50% probability *adhav* = 0.90 *adhvar* = 0.06, 20% probability *adhav* = 0.95 *adhvar* = 0.05)

Adherence pattern 4 (30% probability *adhav* = 0.50 *adhvar* = 0.2, 30% probability *adhav* = 0.70 *adhvar* = 0.2, 10% probability *adhav* = 0.90 *adhvar* = 0.06, 30% probability *adhav* = 0.95 *adhvar* = 0.05)

Adherence pattern 5 (30% probability *adhav* = 0.50 *adhvar* = 0.2, 30% probability *adhav* = 0.60 *adhvar* = 0.2, 10% probability *adhav* = 0.70 *adhvar* = 0.06, 30% probability *adhav* = 0.90 *adhvar* = 0.05)

Costs

All costs are in \$1000 per 3 month period in 2013.

Drug costs* below increased by 20%** for supply chain etc (as in b) – costs are annual unless stated

zidovudine: 0.070
tenofovir: 0.048
ddI: 0.100
lamivudine: 0.021
stavudine: 0.024
nevirapine: 0.028
efavirenz: 0.039
lopinavir/r: 0.268
atazanavir/r: 0.219

Mean cost of treatment of a WHO 4 condition over 3 months (cost is incurred for 3 months): 0.200⁺

Mean cost of treatment of a WHO 3 condition over 3 months (cost is incurred for 3 months): 0.020⁺

Mean cost of treatment of TB per 3 months (cost is incurred for 6 months): 0.050⁺

Cotrimoxazole annual cost: 0.005⁺

CD4 count measurement: 0.010^{***+}

Viral load measurement: 0.045^{***+}

Clinic visit cost: 0.020⁺

Resistance test cost: 0.250⁺⁺⁺

HIV test (including personnel costs): 0.010^{**}

* Untangling the web of antiretroviral price reductions. 16th Edition – July 2013. www.msfacecess.org. (17)

** Eaton J et al. How should HIV programmes respond to evidence for the benefits of earlier treatment initiation ? A combined analysis of 12 mathematical models. Lancet Global Health 2013. (18)

***Keebler D, Revill P, et al. How Should HIV Programmes Monitor Adults on ART? A Combined Analysis of Three Mathematical Models. Lancet Global Health 2013. (19)

+ Specific data not available on average unit costs of treating WHO stage 3 and 4 conditions and per clinic visit costs - costs used are informed by evidence synthesis from studies that cost according to current CD4 count of those in pre-ART care, cost of ART initiation, which also include costs of CD4 tests (18.)

+++ estimate of potential lowest feasible cost with centralised testing.

Utilities*

Values are 1 except for the following:

Any drug toxicity in current 3 month period: 0.95

Any WHO 3 condition (except TB) in current 3 month period: 0.78

Current TB in current 3 month period: 0.60

Any WHO 4 condition in current 3 month period: 0.46

* Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2129–43. (20)

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